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ANTIBIOTIC USE AND RESISTANCE

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Every dentist practicing clinical dentistry will, during his or her career, have to deal with an infection. Infection may be the prime driver for patient presentation or may be as a result of a restorative, endodontic, periodontal, or surgical procedure.

In this era of antibiotic overuse, microbial resistance is a growing concern. The benefit of antibiotic prophylaxis in preventing relevant surgical site infections must be balanced with the inherent risks of antibiotic use.

There are numerous studies that have demonstrated the relationship between antibiotic overuse and resistance. The risk of antibiotic prophylaxis both to the individual patient (e.g. gastrointestinal adverse effects, Clostridium Difficile risks, allergic reactions) and to the institution or region (e.g. increased resistance, reduced global efficacy of antibiotics) suggest that this question should not be considered lightly.

The Canadian Minister of Health in the October 2014 publication, *Antimicrobial Resistance and Use in Canada: A Federal Framework for Action* states, "Antimicrobial resistance is a global health concern. The loss of effective antimicrobials is reducing our ability to protect Canadians from infectious disease, with the profound impacts on our health care system, global trade, agriculture, environment, and health sectors." The report focuses on three areas: surveillance, promoting prudent antimicrobial use, and innovation. The Federal Framework emphasizes that provinces, territories, and other stakeholders play key roles in helping to address antimicrobial resistance.

Dentists must be aware of changing trends and continually adapt their practices to serve their patients and society according to currently accepted professional standards. The Alberta Dental Association and College Code of Ethics Article A2: Current/Continued Competence states, "The privilege of dentists to be accorded professional status rests primarily in the knowledge, skill, attitude and judgment with which they serve their patients and society. All dentists, therefore, must keep their knowledge of dentistry current and must provide treatment in accordance with currently accepted professional standards. Dentists have an obligation to maintain competence throughout their career and to comply with the Alberta Dental Association and College's Continuing Competence Program under the *Health Professions Act* of Alberta." It will be necessary for dentists to be knowledgeable of the issues related to drugs prescribed, evaluate existing practices, and adapt as necessary to the current environment of increasing bacterial resistance.

There is a difference between the use of prophylactic antibiotics and the management of an infection of odontogenic origin. Antibiotic prophylaxis entails the use of the appropriate antibiotic administered through the proper route and with the proper timing (within one hour of the incision) and discontinuing the antibiotics within the appropriate time (usually within 24 hours).

Preoperative antibiotics have historically been proposed for two main purposes:

1. To prevent surgical site infections or
2. To prevent bacterial-induced joint prosthetic infection or infective endocarditis in high-risk patients.

The updated guidelines from the American Heart Association now recommend against routine antibiotic prophylaxis for infective endocarditis in dental procedures, except in patients with mechanical cardiac valves, certain congenital heart conditions, cardiac transplantation recipients who develop cardiac valve problems, patients who have received an artificial patch to repair a congenital heart defect within the past 6 months, and patients with previous infective endocarditis.

Similarly, in a recent American Academy of Orthopedic Surgeons and American Dental Association Clinical Practice Guidelines, antibiotic prophylaxis is not recommended for most patients with total joint prostheses. It is the responsibility of the treating dentist or dental to contact the patient's family physician, cardiologist, cardiac surgeon, or orthopedic surgeon if he or she is not certain that prophylaxis is required before initiating any treatment that would produce a bacteremia.

It is critical for Alberta dentists to read and reference the dental section in "*Bugs and Drugs"*, authored by Edith Blondel-Hill and Susan Fryters. Another excellent reference is the "*Medical Letter and Book of Antimicrobial Therapy 19th Edition*".

The need for prophylaxis in surgical procedures of the head and neck region is based on a surgical wound classification.

Table 1: Surgical Wound Classification

CLASS	TYPE	DEFINITION
I	Clean	An uninfected operative wound in which no inflammation is encountered and the respiratory, alimentary, genital, or uninfected urinary tracts are not entered. Clean wounds are closed primarily, and if necessary, drained with closed drainage.
II	Clean-contaminated	Operative wounds in which the respiratory, alimentary, genital, or urinary tracts are entered under controlled conditions, and without unusual contamination.
III	Contaminated	Open, fresh, accidental wounds or incisions in which acute, nonpurulent inflammation is encountered; or, operations with major breaks in sterile technique or gross spillage from the GI tract.
IV	Dirty or Infected	Wounds with existing clinical infection or perforated viscera, and old traumatic wounds with retained devitalized tissues. This category presumes that the organisms causing postoperative infection were present in the operative filed before the operation.

It should be noted that no wound created by dental treatment in the oral cavity is clean. The best classification is Type II: Clean-contaminated, Type III: Contaminated, and Type IV: Dirty or Infected, which are quite often encountered. The management of postoperative infections is predicated on the surgical site and infection type. These are described in Table 2.

Table 2: Surgical-Site Infection Types and Definitions

Surgical Site Infection Type (SSI)	DEFINITION
Superficial	Infection occurs within 30 days after surgery and involves only skin and subcutaneous tissue of the incision and the patient has at least one of the following: 1. Purulent drainage from the superficial incision, 2. Organisms isolate from an aseptically obtained culture of fluid or tissue from the superficial incision, 3. Superficial incision that is deliberately opened by a surgeon and is culture-positive or not cultured and patient has at least one of the following signs or symptoms: pain or tenderness, localized swelling, redness, or heat. A culture-negative finding does not meet this criterion and/or 4. Diagnosis of superficial incisional SSI by the surgeon or attending physician.
Deep incisional	Infection occurs within 30 or 90 days after the operations and involves deep soft tissues of the incision (i.e., fascial and muscle layers) and the patient has at least one of the following: 1. Purulent drainage from the deep incision, 2. A deep incision that spontaneously dehisces or is deliberately opened by the surgeon and is culture-positive or not cultured, and patient has at least one of the following: fever (>38 C), localized pain, or tenderness. A culture- negative finding does not meet this criterion, 3. An abscess or other evidence of infection involving the deep incision that is found on direct examination, during an invasive procedure, or by histopathologic examination or imaging test and/or 4. Diagnosis of deep incisional SSI by a surgeon or attending physician.
Organ/space	Infection occurring with 30 or 90 days after the operation and infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure and the patient has at least one of the following: 1. Purulent drainage from a drain that is placed into the organ/space, 2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space, 3. An abscess or other evidence of infection involving the organ/space that is found on direct examinations. during invasive procedure, or by histopathologic examination or imaging test, 4. Diagnosis of an organ/space SSI by a surgeon or attending physician and/or 5. Meets at least one criterion for a specific organ/space infection site (e.g. bone, breast abscess or mastitis, ear, mastoid, oral cavity, sinusitis).

In preparing for this article, I was in contact with Dr. A. Mark Joffe, Senior Medical Director, Infection Prevention and Control, Alberta Health Services and Infectious Diseases Consultant at the Royal Alexandra Hospital. He shared his experiences with a patient that he had recently managed.

The case revolves around a male patient in his 70s, generally in excellent health. He had a dental extraction for unknown reason; he had no pain, no problem that he was aware of, and he was not sure why the tooth needed to be extracted (it sounds as if there was not an associated abscess). He was prescribed a 10-day course of clindamycin following the extraction. He took it exactly as instructed. Midway through the course, he developed diarrhea. He had not been warned about this possibility and continued to take his clindamycin as instructed. By the end of the course, he was having more than 10 bowel movements per day, and he became delirious. He was taken to the Sturgeon Hospital in St. Albert where he resided. At the hospital, it was discovered he was in acute renal failure and had a creatinine level of 850, on the basis of diarrhea/dehydration due to Clostridium Difficile. He was admitted to the ICU with renal failure which required dialysis. He was ultimately transferred to the Royal Alexandra Hospital after 10 days in the ICU at the Sturgeon. This is where Dr. Mark. Joffe became involved. It was feared that he would need long-term dialysis.

His kidneys gradually and slowly recovered. He spent a month in the Royal Alexandra Hospital receiving dialysis for the first several weeks of his stay and was gradually tapered off. The end result was reasonably good, but things were pretty tough for this man and it could have worked out a lot worse; fortunately, his kidneys did recover or he would be looking at dialysis for the rest of his life. In the meantime, he had an approximately 6-week hospitalization including 10 days in the ICU -a huge cost to the system. Dr. Joffe reported that he is quite sure that his original dentist had no idea that any of this had happened. He will never know that a clindamycin prescription probably was not indicated in the first place and had a huge impact on this man, his family, and our health care system. Dr. Joffe went on to say, "We are seeing tons of C. Difficile. Nobody tracks it well but there is significant use of Clindamycin in the community, a lot of it by Dentists, and some of the C. Diff. we're seeing is a consequence. To be clear, some of this is just bad luck but some of it follows use of antibiotics in dentistry where it may not be needed and where Clindamycin may not be the first or optimal choice."

In order for the treating dentist to determine when antibiotics should be used, he or she should be aware of the patient's medical history. A thorough review of allergies is essential. Many patients claim to be allergic to antibiotics. It is essential to determine what the allergic reaction is. The worst type of allergic reaction is the IgE acute reaction that results in anaphylaxis. A recent review in regards to cross reactivity between penicillins and cephalosporins reported that there is approximately a 1 percent cross reactivity in individuals who reported a penicillin allergic reaction and a 2.5 percent cross reactivity in those with a confirmed penicillin allergy. Third and fourth generation cephalosporins and those with different beta-lactam R1 side chains can be used safely in penicillin-allergic patients.

To treat infection, it is essential to understand the anatomy of infection spread, surgical anatomy

for appropriate drainage, and the microbiology involved in the infection or, in the case of prophylaxis, the organism expected to be encountered. Antibiotics are an adjunct to overall patient management and do not replace the age-old adage of eliminating the cause and draining the pus. The knowledge of surgical anatomy, microbiology, bacterial resistance, and appropriate antibiotic use is the responsibility of every dentist in the province. If a patient experiences an infection that requires the expertise of a surgical specialist, then the dentist must make direct contact with this specialist to transfer care. Sending a patient to the emergency room without this direct transfer of care constitutes patient abandonment and violates the ethical standards of the Alberta Dental Association and College.

If any Dental practitioner really wants to know what is happening with resistance, they can assess real data from the Dynalife lab Antibiogram that is updated regularly.
Website: http://www.dynalifedx.com/HealthProfessionals/Antibiograms/tabid/1317/Default.aspx.

This information comes from the Edmonton area, excluding the University Hospital. Data for Northern Alberta (i.e. outside of Edmonton) are also available. Calgary Lab Services offers a similar website for the Calgary area. http://www.calgarylabservices.com/education-research/publications/microbiology-newsletters.aspx

To pick a couple of relevant examples, Streptococcus anginosus (a very common abscess-producing organism of mouth/gut origin) is 87 percent susceptible to Clindamycin in Calgary and 76 percent in Edmonton. (These results are based on just 93 isolates from Calgary and 33 from Edmonton.) Viridans group Strep are 79 percent susceptible to Clindamycin in Edmonton but this is based on only 14 isolates that were grown from blood. There is no similar info. available from Calgary.

There is a sense in the infectious disease community that 20 percent of all odontogenic infections are resistant to clindamycin. In cases where multiple doses of antibiotics had been administered, this resistance can be as high as 40 percent.

Amoxicillin is a good first-line choice to manage dental infections. Amoxicillin/clavulin is a good second choice in patients with minimal or no improvement. The clavulanic acid part of this drug extends the coverage to all anaerobes, so there would be no need to add metronidazole (Flagyl) if that drug is used. Amoxicillin and Flagyl would give a good, broad range spectrum coverage.

If there is still a failure to respond, then IV ceftriaxone or even penicillin/amoxicillin plus Flagyl can be used for less severe infections. Ertapenem and Piptazo are very broad spectrum antibiotics given intravenously and have particularly good gram-negative coverage.

In the case of the true penicillin allergy, thoughts could be given to the use of cephalosporins as the first-line treatment and the use of cephalosporins with Flagyl if there is a treatment failure. Clindamycin can be used, but its use and side effects need to be closely monitored.

All antibiotics can produce antibiotic-induced colitis. Clindamycin has been implicated more often than the others.

All patients should be informed of the possibility of diarrhea with the use of antibiotics and should be informed to call the prescriber's office to discuss this problem should this situation develop.

Table 3: Common Antibiotics Used Orally		
DRUG	**ADULT DOSE**	**PEDIATRIC DOSE**
Amoxicillin	250 mg q8h or 875 mg q12h	20 to 30 mg/kg per day in divided doses
Amoxicillin Clavulin	500/125 mg bid or tid and 875/125 mq bid or tid	125/28.5 mg – 200/28.5 mg q8h
Cephalosporins 1st Generation	**ADULT DOSE**	**PEDIATRIC DOSE**
Cefadroxil	1-2 g per day	<1 year: 30 mg/kg per day divided in two doses every 12h
Cephalexin (Cephalex, Novolexin, Keflex)	250-500 mg q6h up to 4 g q6h in severe infections	25-50 mg/kg per day in divided doses q6h
Cephalosporins 2nd Generation	**ADULT DOSE**	**PEDIATRIC DOSE**
Cefaclor (Apo Cefaclor)	250-500 mg q8h	20-40 mg/kg per day in divided doses q6h
Cefprozil (Cefzil)	250-500 mg every 12 to 24h	50 mg/kg q12h
Cefuroxime/Axetil (Ceftin)	250-500 mg q12h	<12 years: 125 mg q12h >12 years: 250-500 mg q12h
Cephalosporins 3rd Generation	**ADULT DOSE**	**PEDIATRIC DOSE**
Cefixime (Suprax)	200-400 mg every 12 to 24 hours	<12 years: 4-8 mg/kg q12h >12 years: 200 mg to 400 mg every 12 to 24 hours
DRUG	**ADULT DOSE**	**PEDIATRIC DOSE**
Clindamycin	150-300 mg q6h	3-6 mg/kg q6h
DRUG	**ADULT DOSE**	**PEDIATRIC DOSE**
Metronidazole (Flagyl)	250-500 mg q12h	35-50 mg/kg q24h
DRUG	**ADULT DOSE**	**PEDIATRIC DOSE**
Penicillin VK	250-500 mg q6h	<12 years: 50-75 mg/kg per day divided every 6 to 8 hours not to exceed 3 g per day >12 years: 300-600 mg q6h